Remarks

The Examiner indicates that in the current application, claims 2-4, 13-15, 49, 52, 60, 61 and 70 are being considered and are finally rejected. Applicants respectfully request that claims 5-9, 16, 17, 50, 51, 53-57, 62 and 63 which were subjected to election of species, be rejoined with the currently considered claims. Claims 2 and 49 have been amended.

Claim Rejection Under 35 USC §103

Claims 2-4, 14, 15, 49-52 and 60-61 and 70 as being obvious over Shepard et al. (April 2000) in view of Grovit-Ferbas et al.(July 2000)

Applicants agree with the Examiner that Shepard et al. do not teach purifying non-pathogenic microorganism by covalent attachment of a compound to surface proteins (and note that such covalent attachment is not a purification technique) but disagree that the invention is obvious over Shepard et al. in view of Grovit-Ferbas et al. In this regard, the Examiner has correctly pointed out that Grovit-Ferbas et al. teach chemical treatment of HIV-1 using formaldehyde and viral purification by ultrafiltration. However, it is asserted in the Office Action that it would have been obvious to modify the sample of Shepard et al. by modifying the virus-containing biological sample disclosed therein with the chemical treatment as taught by Grovit-Ferbas et al. (see page 3 of the Office Action, reiterating the rejection of July 14, 2006).

In response, Applicants point out that the plain meaning of the present claims requires that the organism to be rendered non-pathogenic via the irreversible modification of one or more surface proteins by covalent attachment of a compound comprising one or more reactive functional groups to one or more reactive sites on said surface proteins. Therefore, the non-pathogenicity of the present method is achieved without the use of thermal treatments. "Non-pathogenic" is defined in the present application to mean that "as a result of the modification of the surface proteins according to the methods of the invention, the microorganism is not able to infect cells, replicate or cause disease despite having its nuclear contents substantially intact." (page 7, lines 19-22). Grovit-Ferbas et al. do not disclose rendering a virus non-pathogenic without the use of thermal treatment. Therefore, one skilled in the art, upon reading Grovit-Ferbas et al., would not suspect that the chemical treatments disclosed therein would render the virus non-pathogenic as the term is used in the instant case. Nonetheless, Applicants point out that, in contrast to the instant claims, inactivating a virus present in the biological sample of Shepard et al.

would not result in a *purified* microorganism in a liquid matrix comprising biological fluid, particularly wherein the microorganism is required to be purified *prior* to suspension in the liquid matrix as the instant claims require. Specifically, the HIV-1 particles in the samples disclosed by Shepard et al. are present at the time the samples are obtained from infected individuals (see, for example, Tables 1 and 2, p1415); adding formaldehyde to such samples as taught by Grovit-Ferbas et al. would not result in a *purified* microorganism, nor could it be correctly stated that such microorganisms would have been purified *prior* to suspension in the liquid matrix, nor would one expect the particles to be non-pathogenic. Therefore, even if one skilled in the art were to combine the teachings of Grovit-Ferbas et al. Shepard et al. as has been done in the Office Action (which Applicants submit would not be done by one skilled in the art), it would still not result in the present invention, or even in an obvious variant thereof.

Applicants also disagree that one would be motivated to modify the positive control of Shepard et al. by replacing it with the chemically modified virus of Grovit-Ferbas et al. Specifically, Shepard et al. utilize internal positive controls (see page 1415, first two full paragraphs, right column). Adding the chemically modified virus of Grovit-Ferbas et al. to the samples describe by Shepard et al. would not provide a "control" since the added virus would merely increase the molarity of RT-PCR primer binding sequences in the sample. Thus, it is unclear to Applicants how the Examiner envisions that, by adding more of the target virus to the sample of Shepard et al., one could utilize the added virus as an amplification "control." Therefore, it is respectfully submitted that one could not form a reasonable expectation in arriving at the present invention from the cited combination of references. Nevertheless, it is also noted that Applicants' previous response has been deemed unpersuasive in part because certain features that were presumably distinct from the cited references were allegedly not recited in the previously pending claims (see page 5 of the Office Action, last full paragraph). Therefore, in response, Applicants have amended claim 2 to specify that the composition is suitable for use as a positive control for nucleic acid amplification after storage at a temperature between and including 2-8°C, and have amended claim 49 to specify that the kit of the invention has been stored at a non-frozen temperature. Basis for these amendments can be found in a number of places in the specification (see, for one example, page 3, lines 21-29).

In view of the foregoing arguments and amendments, Applicants courteously submit that the combination of Grovit-Ferbas et al. and Shepard et al. do not teach or even suggest a

composition comprising a *purified* microorganism in a liquid matrix comprising biological fluid, wherein the microorganism is purified *prior* to suspension in the liquid matrix, wherein the composition is suitable for use as a positive control for nucleic acid amplification, and wherein the microorganism is non-pathogenic. Applicants emphasize that the use of positive controls in nucleic acid amplification based methods for detecting the presence of microorganisms is critical for accurate results, and that the compositions as now recited in claim 2 can be stored as 2-8°C and yet maintain the ability to serve as a positive control material. None of these features are disclosed or even suggested in the cited references. Therefore, Applicants assert that the cited references do not teach, motivate or suggest the compositions as recited in instant claims.

Based on the above arguments, Applicants respectfully assert that the presently claimed compositions are not obvious in view of the cited references.

Claims 2-4, 14, 15, 49-52 and 60-61 and 70 as being obvious over Shepard et al. (April 2000) in view of Grovit-Ferbas et al., July 2000) and further in view of Norman et al. (1970)

The references of Shepard et al. and Grovit-Ferbas et al. have been discussed above. Applicants respectfully submit that, since the presently claimed invention is patentable over the references of Shepard et al. and Grovit-Ferbas et al., the additional teaching of adding sucrose to pathogenic mycoplasma in Norman et al. is inadequate to maintain the rejection of the now pending claims which require, among other elements as noted above, a liquid matrix comprising a biological fluid.

Therefore, Applicants respectfully assert that none of the references cited by the Examiner suggest or motivate the current composition which comprises: a purified microorganism which has been rendered non-pathogenic by covalent linkage of surface proteins and is suspended in a liquid matrix after purification, wherein the liquid matrix comprises a biological fluid, and wherein the nucleic acids are amenable to amplification after storage at a temperature between and including 2-8°C.

Conclusion

Based on the amendments and the arguments presented herein, Applicants believe the claims are now in a condition for allowance and therefore request the Examiner to allow these claims.

This response and RCE request is being filed with a request for a three month extension. Checks for $1020 (for the three month extension) and $790 (for the RCE) are enclosed. Any additional fee maybe charged to Deposit Account No. 08-2442.

Respectfully submitted,

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